

Application No.: 09/913,419

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AMENDMENTS TO THE CLAIMS

1. (currently amended) An isolated cytokine-binding domain of Domain 4 of a  $\beta_c$  chain or analogous structure of a cytokine receptor, or portion thereof, which binds to at least one cytokine and is capable of transducing a cytokine signal through a single cytokine receptor, said domain comprising a portion of the B'-C' loop of the cytokine binding domain comprising a region defined by an N-terminus of Domain 4 and by a B'-C' loop including residues Tyr365, His367, and Ile368 of Domain 4 of the  $\beta_c$  chain.
2. (currently amended) The cytokine binding cytokine-binding domain according to claim 1 comprising a portion of the B'-C' loop of domain Domain 4 and a groove which is defined by the B'-C', F'-G' loops, and wherein the F'-G' loop comprises residues 418 and 421 of Domain 4 of the  $\beta_c$  chain, and the N-terminal section of Domain 4.
3. (currently amended) The cytokine binding cytokine-binding domain according to claim 1 further including a Tyrosine residue capable of interaction with an  $\alpha$  chain subunit or with Domain 3 of the  $\beta$   $\beta_c$  chain subunit to allow high affinity binding of the cytokine.
4. (currently amended) The cytokine binding cytokine-binding domain according to claim 3 wherein the tyrosine is Tyr421 or equivalent residue of an analogous common signalling structure.
5. (currently amended) The cytokine binding cytokine-binding domain according to claim 1 wherein the B'-C' loop residues of Domain 4 of the  $\beta_c$  chain comprises residues 365 to 368 forming a type 1  $\beta$ -turn or an analogous structure in an analogous common signalling structure.
6. (currently amended) The cytokine binding cytokine-binding domain according to claim 1 wherein the binding domain of the  $\beta_c$  chain, or portion thereof which binds to at least one cytokine, is defined by an area bordered by any one of the following residues including Lys362, Tyr365, His367, Ile368, Arg418, Gly420, Asn422, Thr416, Ile338, Gln339, Met340 and Met361 or equivalent residues in an analogous common signalling structure of a cytokine receptor.

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7. (canceled)

8. (currently amended) The cytokine binding cytokine-binding domain according to claim 1 that binds to at least two cytokines selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13.

9. (canceled)

10. (currently amended) The cytokine binding cytokine-binding domain according to claim 9 claim 1 wherein the common β<sub>c</sub> chain is derived from a receptor selected from the group consisting of IL-5 receptor, IL-3 receptor and GM-CSF receptor.

11. (currently amended) The cytokine binding cytokine-binding domain according to claim 2 wherein the F'-G' loop adopts a type IVβ turn ~~at its tip in Domain 4 and includes the residues Arg418 and Tyr421.~~

12. (currently amended) A method of identifying a compound having cytokine agonist or antagonist activity which comprises:

subjecting a potential cytokine agonist and/or cytokine antagonist compound to the cytokine binding domain ~~or portion thereof~~ according to claim 1; and

determining the presence of an agonist or antagonist response to the compound on the activity of a cytokine.

13. (currently amended) A method of identifying a compound having a cytokine agonist or antagonist activity, which comprises:

subjecting a potential cytokine antagonist to the cytokine binding domain ~~or portion thereof~~ according to claim 1; and

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identifying a compound that has bound to the cytokine-binding domain wherein said compound has an agonist or antagonist response on the activity of the cytokine.

14. (currently amended) A The method according to claim 12 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

15. (currently amended) A The method according to claim 12 wherein the cytokine agonist or antagonist further binds to ~~Tyr421 or an equivalent residue of a common signalling unit of a cytokine receptor.~~

16. (previously presented) A cytokine agonist or antagonist identified by a method according to claim 12.

17. (previously presented) An antibody or fragment thereof to the cytokine binding domain according to claim 1.

18. (currently amended) The cytokine binding domain according to claim 1 comprising a mutation directed to ~~any one of the residues~~ a residue selected from ~~the~~ a group including consisting of Gln340, Ile338 and Met361 ~~or an equivalent residue of a common signalling unit of a cytokine receptor of Domain 4 of the  $\beta_c$  chain.~~

19. (original) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an agonist or antagonist according to claim 16.

20. (original) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an antibody according to claim 17.

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21. (currently amended) The method according to claim 19 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma, leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia, and wherein said cytokine agonist or antagonist is an antagonist.

22. (previously presented) The method according to claim 20 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma, leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia.

23. (currently amended) The method according to claim 19 wherein the cytokine-related condition is allergic inflammation and the antagonist inhibits the binding of any one of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

24. (currently amended) The method according to claim 20 wherein the cytokine-related condition is allergic inflammation and the antagonist antibody inhibits the binding of any one of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

25. (previously presented) The method according to claim 23 wherein the allergic inflammation results in asthma.

26. (previously presented) The method according to claim 24 wherein the allergic inflammation results in asthma.

27. (previously presented) The method according to claim 19 wherein the cytokine-related condition is selected from the group including hemopoiesis, boosting immune response, suppression of embryonic stem cell differentiation, immunostimulation, antitumor activity, expansion of early

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hemopoietic cells, anemia, correcting thrombocytopenia, wherein said cytokine agonist or antagonist is an agonist.

28. (previously presented) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5 GM-CSF, IL-4, or IL-13 response.

29. (currently amended) The method according to claim 13 wherein the cytokine agonist or antagonist further binds to Tyr421 or an equivalent residue of a common signalling unit of a cytokine receptor.

30. (previously presented) A cytokine agonist or antagonist identified by a method according to claim 13.

31. (new) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

32. (new) The cytokine-binding domain according to claim 1 which comprises a hydrophobic patch, said patch having residues selected from a group consisting of Ile338, Ala341, Met361, and Tyr365 of Domain 4 of the  $\beta_c$  chain.

33. (new) The cytokine-binding domain according to claim 31 comprising Met340 and Pro342 of the  $\beta_c$  chain.

34. (new) The cytokine-binding domain according to claim 31 comprising Ile368 or Tyr421 of the  $\beta_c$  chain.

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35. (new) The cytokine-binding domain according to claim 13 comprising Ile368 or Tyr421 of the  $\beta_c$  chain.

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